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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/900,627,

07/06/2001

Charles David Weaver

3035-4086US1

7563

23914

7590

02/22/2005

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EXAMINER

CHEU, CHANGHWA J

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 02/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/900,627	WEAVER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Jacob Cheu	1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 November 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-120 is/are pending in the application.
- 4a) Of the above claim(s) 32-120 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Applicant's amendment filed on 11/24/2004 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

Claims 1-31 are currently under examination. Claims 32-120 are withdrawn from further consideration.

#### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The instant invention directs to an apparatus for measuring cellular electrical conditions, such as transmembrane potential, capacitance, resistance and conductance. The apparatus comprises two layers. The first layer comprising a non-conductive material comprising a top and

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bottom surface and including pores, wherein the top surface containing cell attachment sites configuring that the pores being spaced apart such only one pore may contact an individual cell, and the pores are capable of forming electrically tight seals with the contacted cells at the cell attachment sites. The second layer comprises a non-conductive, sealant material which contacts the first layer and spans across at least one pore.

The apparatus is designed to study the cellular electrophysiology responses. However, in view of the specification and the prior arts, the instant invention raises issue of enablement to one ordinary skilled in the art to use the claimed apparatus with undue experimentation and lack of predictability.

The apparatus mainly comprises two layers. The first layer has pores “each *extending between, and through*, said top and bottom surfaces, wherein the top surface of the material comprises one or more cell attachment sites which circumscribes each of the pores of the material and contact the cells”. The second layer for this apparatus has the feature of “comprising a *non-conductive*, sealant material which contacts the first layer of the cell support membrane and *spans across* at least one pore” (emphasis added). However, applicant states in the specification that the second layer is removed by laser ablation or enzymatic digestion. For example, page 15, line 20-30, the layer is “capable of being removed, solubilized, or made conductive at regions that contact the pores of the porous layer upon exposure to an enzyme or laser illumination”. Page 16, line 18-25, applicant states that the layer can be removed by ‘contact an enzyme, ..... suitable enzymes include, but not limited to, enzymes that digest proteins or sugar polymer, for example, proteases, cellulases, esterases, and depolymerase.” Furthermore, applicant demonstrates the working examples, i.e. example 5-7, to remove the second layer for conducting cellular electrophysiology study. In example 7, applicant states that “[w]here cells are attached to the pores of the cell support membrane, the secreted enzyme molecules diffuse through the pores to contact, digest, and remove the cellulose sealant layer. This *allows electrical measurements* of the attached cells.” (See page 34, Example 7)(emphasis added). The aforementioned information nevertheless indicates that the instant apparatus can function at the condition where the second layer (a non-conductive material) contacting the pore

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(where cells attached) is removed, not as the recited feature where this non-conductive material spans across the pores because there would be no flow of electricity for the non-conductive second layer if it spans across the pores.

In addition, several prior arts designed to measure the cellular electrical conditions have the free flow of electricity through the pores upon which cells attached. For example, Owen et al. (WO 99/66329) teach an apparatus to measure transmembrane potential, i.e. ion channels. The device taught by Owen et al. has similar features of plurality of pores spaced apart for attachment of individual cell where there is electrolyte solution beneath the pores for measuring the electrical condition of the cells in response to the impact of a compound (See Figure 1-8). Similarly, Byrne et al. (WO 00/34776) teach using patch clamp technique to measure the whole cell electrical activity. Byrne et al. teach using a plurality of micropatches on a membrane layer to measure the cell electrical activity (See Figure 23-25). The pores on the membrane can be attached by a single cell and measured by the electrodes (See Figure 25). The pores are not blocked, e.g. no second layer spanning across, so that there would be free electrical flow through the pores for measurement. Furthermore, Meyer et al. (US 6379916) also teach a patch-clamp method for measuring cell electrical activities. The arrangement of the device is that each pore can be occupied by a single cell and measured by electrodes (See Figure 1-3; Particular Figure 2). Note, Figure 4, component 4 beneath the plurality of pores are filters which are permeable to electrolyte solution. Taken together, the instant invention can function according to its purported purpose, i.e. measuring cellular electrical conditions, not with a second layer which contact the first layer containing pores where the second layer spans across the pores.

In view of the aforementioned lack of predictability in the art, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in the applicant's specification of how to effectively practice the recited method and absent working examples.

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***Response to Applicant's Arguments***

3. Applicant's arguments with respect to claims 1-31 have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-282-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu  
Examiner  
Art Unit 1641



January 25, 2005



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02/17/05